

CLAIMS

(000703) What is claimed is:

(000704) 1. A pharmaceutical formulation comprising one or more excipients and 3 α ,16 α ,17 β -trihydroxy-5 α -androstane, 3 α ,16 α -dihydroxy-17-oxo-5 α -

5 androstane, 3 β ,16 α ,17 β -trihydroxy-5 α -androstane, 3 β ,16 α -dihydroxy-17-oxo-5 α -androstane, 3 α ,16 β ,17 β -trihydroxy-5 α -androstane, 3 α ,16 β -dihydroxy-17-oxo-5 α -androstane, 3 β ,16 β -dihydroxy-17-oxo-5 α -androstane, 3 α ,16 α ,17 β -trihydroxy-5 β -androstane, 3 α ,16 α -dihydroxy-17-oxo-5 β -androstane, 3 β ,16 α ,17 β -trihydroxy-5 β -androstane, 3 β ,16 α -dihydroxy-17-oxo-5 β -androstane, 3 α ,16 β ,17 β -trihydroxy-5 β -
10 androstane, 3 α ,16 β -dihydroxy-17-oxo-5 β -androstane, 3 β ,16 β -dihydroxy-17-oxo-5 β -androstane or a 2-oxa, 11-oxa or 19-nor analog of any of these compounds.

(000705) 2. The pharmaceutical formulation of claim 1 wherein the compound is 3 α ,16 α ,17 β -trihydroxy-5 α -androstane.

(000706) 3. The pharmaceutical formulation of claim 1 wherein the
15 compound is 3 α ,16 α -dihydroxy-17-oxo-5 α -androstane.

(000707) 4. A pharmaceutical formulation for buccal or sublingual administration comprising one or more excipients and a compound wherein the compound is 16 α -fluoro-17-oxoandrost-5-ene, 3 α -hydroxy-16 α -fluoro-17-oxoandrost-5-ene, 3 β -hydroxy-16 α -fluoro-17-oxoandrost-5-ene 7 α -hydroxy-16 α -
20 fluoro-17-oxoandrost-5-ene, 7 β -hydroxy-16 α -fluoro-17-oxoandrost-5-ene, 16 α -fluoro-7,17-dioxoandrost-5-ene.

(000708) 5. The pharmaceutical formulation of claim 4 wherein the compound is micronized.

(000709) 6. The pharmaceutical formulation of claim 4 wherein the
25 compound is 16 α -fluoro-17-oxoandrost-5-ene.

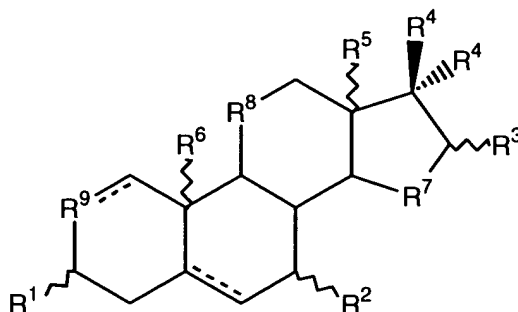
(000710) 7. A pharmaceutical formulation comprising one or more excipients and two or more of 3 β -hydroxy-16 α -bromo-17-oxo-5 α -androstane, 3 β -hydroxy-16 β -bromo-17-oxo-5 α -androstane and 3 β -hydroxy-16 α -bromo-17-oxo-5 α -androstane hemihydrate.

(000711) 8. The pharmaceutical formulation of claim 7 wherein the pharmaceutical formulation is for oral, buccal, sublingual or aerosol administration.

(000712) 9. The pharmaceutical formulation of claim 7 comprising 7 β -hydroxy-16 β -bromo-17-oxo-5 α -androstane and 3 β -hydroxy-16 α -bromo-17-oxo-5 α -androstane hemihydrate.

(000713) 10. The pharmaceutical formulation of claim 9 wherein the pharmaceutical formulation is for oral, buccal, sublingual or aerosol administration.

(000714) 11. A method to increase the numbers or activity of neutrophils, dendritic cells, macrophages or monocytes in a human or a primate having or subject to developing an innate immune suppression condition or a symptom thereof comprising administering an effective amount of a compound having the formula



(000715)

(000716) wherein the dotted lines are optional double bonds and when hydrogen is present at the 5-position, it is in the α -configuration;

15 (000717) R^1 is $-OR^{PR}$, $-SR^{PR}$, $-N(R^{PR})_2$, $-O-Si-(R^{13})_3$, an ester, a thioester, a phosphoester, a phosphothioester, a phosphonoester, a sulfite ester, a sulfate ester, an amino acid, a peptide, an ether, a thioether, a carbonate, a carbamate, an optionally substituted monosaccharide or an optionally substituted oligosaccharide;

(000718) R^2 and R^3 independently are $-H$, $-OR^{PR}$, $-SR^{PR}$, $-N(R^{PR})_2$, $-O-Si-(R^{13})_3$, $-CN$, $=O$, $=S$, $=NOH$, an ester, a thioester, a phosphoester, a phosphothioester, a phosphonoester, a sulfite ester, a sulfate ester, an amino acid, a peptide, an ether, a thioether, an acyl group, a thioacyl group, a carbonate, a carbamate, a thioacetal, a halogen, an optionally substituted heteroaryl moiety, an optionally substituted monosaccharide or an optionally substituted oligosaccharide;

25 (000719) R^4 independently are $-H$, $-OR^{PR}$, $-SR^{PR}$, $-N(R^{PR})_2$, $-O-Si-(R^{13})_3$, $-CN$, $=O$, $=S$, $=NOH$, an ester, a thioester, a phosphoester, a phosphothioester, a

phosphonoester, a phosphiniester, a sulfite ester, a sulfate ester, an amide, an amino acid, a peptide, an ether, a thioether, a carbonate, a carbamate, a thioacetal, an alkyl group, an optionally substituted alkenyl group, an optionally substituted alkynyl group, an optionally substituted aryl moiety, an optionally substituted heteroaryl moiety, an optionally substituted monosaccharide or an optionally substituted oligosaccharide, provided that both R^4 are not -H;

(000720) R^5 and R^6 independently are -H, an acyl group, a thioacyl group, a halogen, an optionally substituted alkyl group, an optionally substituted alkenyl group or an optionally substituted alkynyl group;

(000721) R^7 is $-\text{CHR}^{10}-$, $-\text{CHR}^{10}-\text{CHR}^{10}-$, $-\text{CHR}^{10}-\text{CHR}^{10}-\text{CHR}^{10}-$, $-\text{CHR}^{10}-\text{O}-\text{CHR}^{10}-$, $-\text{CHR}^{10}-\text{S}-\text{CHR}^{10}-$, $-\text{CHR}^{10}-\text{NR}^{\text{PR}}-\text{CHR}^{10}-$, $-\text{O}-$, $-\text{O}-\text{CHR}^{10}-$, $-\text{S}-$, $-\text{S}-\text{CHR}^{10}-$, $-\text{NR}^{\text{PR}}-$ or $-\text{NR}^{\text{PR}}-\text{CHR}^{10}-$, where R^{10} independently are -H, $-\text{OR}^{\text{PR}}$, $-\text{SR}^{\text{PR}}$, $-\text{N}(\text{R}^{\text{PR}})_2$, $-\text{O}-\text{Si}(\text{R}^{13})_3$, $-\text{CN}$, $=\text{O}$, $=\text{S}$, $=\text{NOH}$, $=\text{CH}_2$, an ester, a thioester, a phosphoester, a phosphothioester, a phosphonoester, a phosphiniester, a sulfite ester, a sulfate ester, an amide, an amino acid, a peptide, an ether, a thioether, an acyl group, a thioacyl group, a carbonate, a carbamate, a thioacetal, a halogen, an optionally substituted alkyl group, an optionally substituted alkenyl group, an optionally substituted alkynyl group, an optionally substituted aryl moiety, an optionally substituted heteroaryl moiety, optionally substituted monosaccharide or optionally substituted oligosaccharide;

(000722) R^8 and R^9 independently are $-\text{CHR}^{10}-$, $-\text{CHR}^{10}-\text{CHR}^{10}-$, $-\text{O}-$, $-\text{O}-\text{CHR}^{10}-$, $-\text{S}-$, $-\text{S}-\text{CHR}^{10}-$, $-\text{NR}^{\text{PR}}-$ or $-\text{NR}^{\text{PR}}-\text{CHR}^{10}-$, or R^8 or R^9 independently is absent, leaving a 5-membered ring-, where R^{10} independently are -H, $-\text{N}(\text{R}^{\text{PR}})_2$, $-\text{CN}$, $=\text{NOH}$, $=\text{CH}_2$, an amide, an acyl group, a thioacyl group, a halogen, an optionally substituted alkyl group, an optionally substituted alkenyl group, an optionally substituted alkynyl group, an optionally substituted aryl moiety or an optionally substituted heteroaryl moiety;

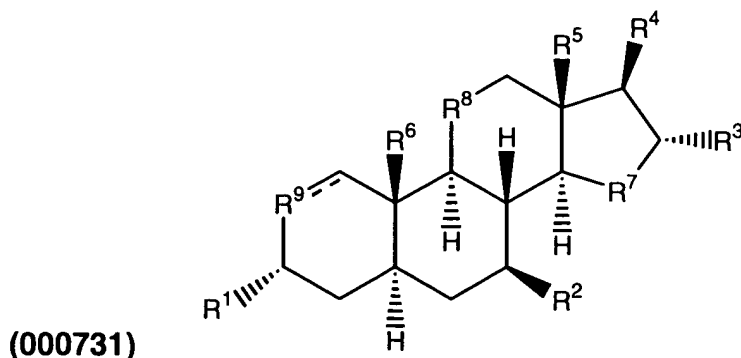
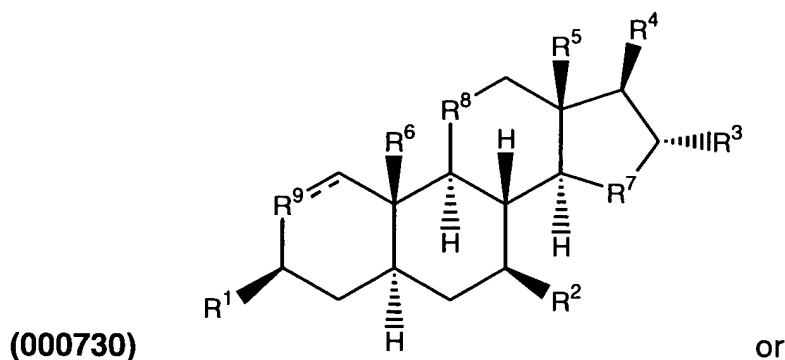
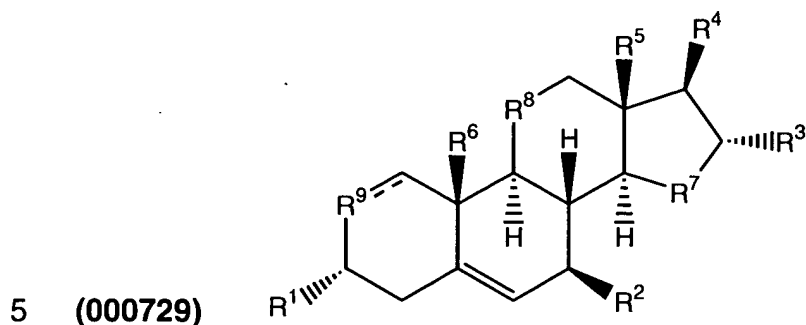
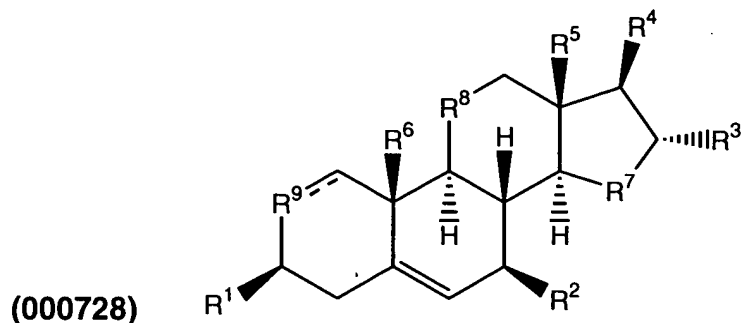
(000723) R^{13} independently are C_{1-6} alkyl; and

(000724) R^{PR} independently are -H or a protecting group.

(000725) 12. The method of claim 11 wherein about 4 to about 40 mg/kg/day, of the compound is administered to the human or the primate.

(000726) 13. The method of claim 12 wherein the compound is intermittently administered to the subject.

(000727) 14. The method of claim 11 wherein the compound has the formula



(000732) 15. The method of claim 14 wherein

- (000733) (1) R¹ and R⁴ are -OH, R² and R³ are -H, R⁵ and R⁶ are -CH₃ and R⁷, R⁸ and R⁹ are -CH₂-; or
- (000734) (2) R¹ and R⁴ are -OH, R² is -H, R³ is -F, -Cl, -Br or -I, R⁵ and R⁶ are -CH₃ and R⁷, R⁸ and R⁹ are -CH₂-; or
- 5 (000735) (3) R¹, R² and R⁴ are -OH, R³ is -H, R⁵ and R⁶ are -CH₃ and R⁷, R⁸ and R⁹ are -CH₂-; or
- (000736) (4) R¹, R² and R⁴ are -OH, R³ is -F, -Cl, -Br or -I R⁵ and R⁶ are -CH₃ and R⁷, R⁸ and R⁹ are -CH₂-; or
- (000737) (5) R¹ is -OH, R² is -H, R³ is -OH, -F or -Br, R⁴ is =O, R⁵ and R⁶ are -CH₃ and R⁷, R⁸ and R⁹ are -CH₂-; or
- 10 (000738) (6) R¹ and R² are -OH, R³ is -H, -F, -Cl or -Br, R⁴ is =O, R⁵ and R⁶ are -CH₃ and R⁷, R⁸ and R⁹ are -CH₂-; or
- (000739) (7) R¹, R³ and R⁴ are -OH, R² is -H, R⁵ and R⁶ are -CH₃ and R⁷, R⁸ and R⁹ are -CH₂-; or
- 15 (000740) (8) R¹, R², R³ and R⁴ are -OH, R⁵ and R⁶ are -CH₃ and R⁷, R⁸ and R⁹ are -CH₂-; or
- (000741) (9) R¹ and R⁴ independently are -OR^{PR}, -SR^{PR}, -N(R^{PR})₂, an ester, a thioester, a monosaccharide, an oligosaccharide, a carbonate or a carbamate, R² and R³ are -H, R⁵ is -CH₃, R⁷, R⁸ and R⁹ are -CH₂-; or
- 20 (000742) (10) R¹ and R⁴ independently are -OR^{PR}, -SR^{PR}, -N(R^{PR})₂, an ester, a thioester, a monosaccharide, an oligosaccharide, a carbonate or a carbamate, R² is -H, R³ is -Br, R⁵ is -CH₃, R⁷, R⁸ and R⁹ are -CH₂-; or
- (000743) (11) R¹ and R⁴ independently are -OR^{PR}, -SR^{PR}, -N(R^{PR})₂, an ester, a thioester, a monosaccharide, an oligosaccharide, a carbonate or a carbamate, R² is -H, R³ is -F, R⁵ is -CH₃, R⁷, R⁸ and R⁹ are -CH₂-; or
- 25 (000744) (12) R¹ and R⁴ independently are -OR^{PR}, -SR^{PR}, -N(R^{PR})₂, an ester, a thioester, a monosaccharide, an oligosaccharide, a carbonate or a carbamate, R² is -H, R³ is -OH, R⁵ is -CH₃, R⁷, R⁸ and R⁹ are -CH₂-; or
- (000745) (13) R¹ and R⁴ independently are -OR^{PR}, -SR^{PR}, -N(R^{PR})₂, an ester, a thioester, a monosaccharide, an oligosaccharide, a carbonate or a carbamate, R² and R³ are -OH, R⁵ is -CH₃, R⁷, R⁸ and R⁹ are -CH₂-; or
- 30

(000746) (14) R^1 and R^4 independently are $-OR^{PR}$, $-SR^{PR}$, $-N(R^{PR})_2$, an ester, a thioester, a monosaccharide, an oligosaccharide, a carbonate or a carbamate, R^2 is $-OH$, R^3 is $-H$, $-F$, $-Cl$ or $-Br$, R^5 is $-CH_3$, R^7 , R^8 and R^9 are $-CH_2-$; or

(000747) (15) R^1 is $-H$, R^2 is $-OH$ or $=O$, R^3 is $-OH$, $-F$, $-Cl$ or $-Br$, R^4 is $-OR^{PR}$, $-SR^{PR}$, $-N(R^{PR})_2$, an ester, a thioester, a monosaccharide, an oligosaccharide, a carbonate or a carbamate, R^5 is $-CH_3$, R^7 , R^8 and R^9 are $-CH_2-$; or

(000748) (16) R^1 and R^2 are $-H$, R^3 is $-OH$ or $=O$, $-F$, $-Cl$ or $-Br$, R^4 is $-OR^{PR}$, $-SR^{PR}$, $-N(R^{PR})_2$, an ester, a thioester, a monosaccharide, an oligosaccharide, a carbonate or a carbamate, R^5 is $-CH_3$, R^7 , R^8 and R^9 are $-CH_2-$; or

(000749) (17) any of (1) through (16) above wherein R^9 is $-O-$ or $-NH-$ instead of $-CH_2-$ or $-CH=$; or

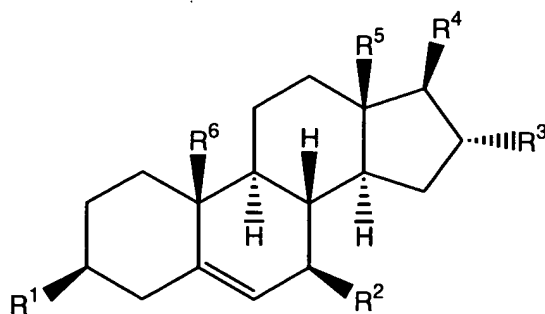
(000750) (18) any of (1) through (17) above wherein R^8 is $-O-$ or $-NH-$ instead of $-CH_2-$; or

(000751) (19) any of (1) through (18) above wherein R^7 is $-O-$, $-NH-$ or $-CHR^{10}-CH_2-$ instead of $-CH_2-$.

(000752) 16. The method of claim 15 wherein about 4 to about 40 mg/kg/day, of the compound is administered to the human or the primate.

(000753) 17. The method of claim 16 wherein the compound is intermittently administered to the subject.

(000754) 18. The method of claim 17 wherein the compound compound has the formula



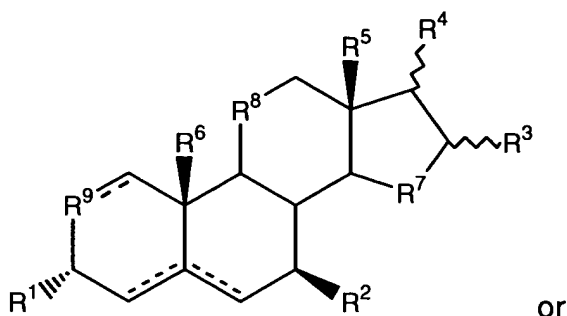
(000755)

(000756) wherein R^1 and R^4 are $-OH$, R^2 and R^3 are $-H$ and R^5 and R^6 are $-CH_3$.

(000757) 19. A method to treat a condition selected from the group consisting of inflammation, osteoporosis, a bone fracture, a wound or trauma and a burn in a

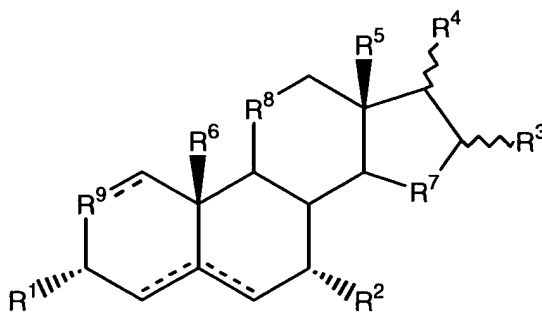
human or a primate having, or subject to developing the condition, wherein the compound has the structure

(000758)

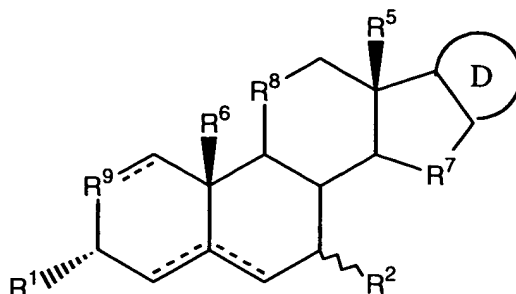


or

(000759)



- 5 (000760) wherein,
- (000761) R¹, R², R³, R⁴, R⁵ and R¹⁰ independently are -H, -OR^{PR}, -SR^{PR}, -N(R^{PR})₂, -N₃, -O-Si-(R¹³)₃, -CN, -NO₂, an ester, a thioester, a phosphoester, a phosphothioester, a phosphonoester, a phosphiniester, a sulfite ester, a sulfate ester, an amide, an amino acid, a peptide, an ether, a thioether, an acyl group, a thioacyl group, a carbonate, a carbamate, a thioacetal, a halogen, an optionally substituted alkyl group, an optionally substituted alkenyl group, an optionally substituted alkynyl group, an optionally substituted aryl moiety, an optionally substituted heteroaryl moiety, an optionally substituted monosaccharide, an optionally substituted oligosaccharide, or,
- 10 (000762) one more of R², R³ and R¹⁰ independently are =O, =S, =NOH or =CH₂, or,
- (000763) R⁴ is =O, =S or =NOH, or,
- (000764) R³ and both R⁴ together comprise a structure having the formula



(000765)

(000766) R⁶ is -H;

(000767) R⁷ is -CHR¹⁰-, -CHR¹⁰-CHR¹⁰-, -CHR¹⁰-CHR¹⁰-CHR¹⁰-, -CHR¹⁰-O-CHR¹⁰-, -CHR¹⁰-S-CHR¹⁰-, -CHR¹⁰-NR^{PR}-CHR¹⁰-, -O-, -O-CHR¹⁰-, -S-, -S-CHR¹⁰-, -NR^{PR}- or -NR^{PR}-CHR¹⁰-;

(000768) R⁸ and R⁹ independently are -CHR¹⁰-, -CHR¹⁰-CHR¹⁰-, -O-, -O-CHR¹⁰-, -S-, -S-CHR¹⁰-, -NR^{PR}- or -NR^{PR}-CHR¹⁰-, or R⁸ or R⁹ independently is absent, leaving a 5-membered ring;

(000769) R¹³ independently is C₁₋₆ alkyl;

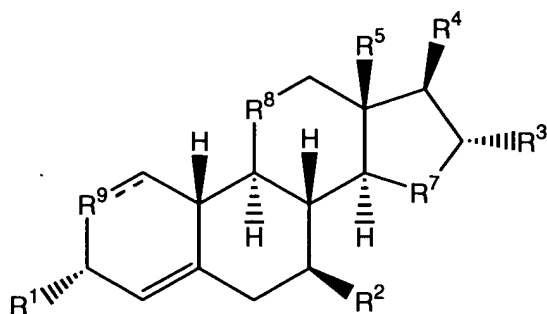
(000770) R^{PR} independently are -H or a protecting group;

(000771) D is a heterocycle or a 4-, 5-, 6- or 7-membered ring that comprises saturated carbon atoms, wherein 1, 2 or 3 ring carbon atoms of the 4-, 5-, 6- or 7-membered ring are optionally independently substituted with -O-, -S- or -NR^{PR}- or where 1, 2 or 3 hydrogen atoms of the heterocycle or where 1 or 2 hydrogen atoms of the 4-, 5-, 6- or 7-membered ring are substituted with -OR^{PR}, -SR^{PR}, -N(R^{PR})₂, -O-Si-(R¹³)₃, -CN, -NO₂, an ester, a thioester, a phosphoester, a phosphothioester, a phosphonoester, a phosphiniester, a sulfite ester, a sulfate ester, an amide, an amino acid, a peptide, an ether, a thioether, an acyl group, a thioacyl group, a carbonate, a carbamate, a thioacetal, a halogen, an optionally substituted alkyl group, an optionally substituted alkenyl group, an optionally substituted alkynyl group, an optionally substituted aryl moiety, an optionally substituted heteroaryl moiety, an optionally substituted monosaccharide, an optionally substituted oligosaccharide, a nucleoside, a nucleotide, an oligonucleotide or a polymer, or,

(000772) one more of the ring carbons are substituted with =O, =S, =NOH, =NOC(O)CH₃ or =CH₂,

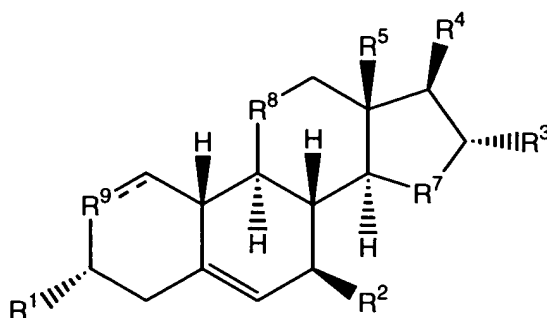
(000773) or D comprises two 5- or 6-membered rings, wherein the rings are fused or are linked by 1 or 2 bonds.

(000774) 21. The method of claim 20 wherein the compound has the structure



5 (000775)

or



(000776)

(000777) 21. The method of claim 20 wherein

(000778) (1) R¹ and R⁴ are -OH, R² and R³ are -H, R⁵ is -CH₃, R⁷, R⁸ and R⁹ are -CH₂-; or

10 (000779) (2) R¹ and R⁴ are -OH, R² is -H, R³ is -Br, R⁵ is -CH₃, R⁷, R⁸ and R⁹ are -CH₂-; or

(000780) (3) R¹ and R⁴ are -OH, R² is -H, R³ is -F, R⁵ is -CH₃, R⁷, R⁸ and R⁹ are -CH₂-; or

(000781) (4) R¹, R² and R⁴ are -OH, R³ is -H, R⁵ is -CH₃, R⁷, R⁸ and R⁹ are -CH₂-; or

(000782) (5) R¹, R² and R⁴ are -OH, R³ is -Br, R⁵ is -CH₃, R⁷, R⁸ and R⁹ are -CH₂-; or

(000783) (6) R¹, R² and R⁴ are -OH, R³ is -F, R⁵ is -CH₃, R⁷, R⁸ and R⁹ are -CH₂-; or

20 (000784) (7) R¹, R³ and R⁴ are -OH, R² is -H, R⁵ is -CH₃, R⁷, R⁸ and R⁹ are -CH₂-; or

- (000785) (8) R^1 , R^2 , R^3 and R^4 are -OH, R^5 is -CH₃, R^7 , R^8 and R^9 are -CH₂-; or
- (000786) (9) R^1 and R^4 independently are -OR^{PR}, -SR^{PR}, -N(R^{PR})₂, an ester, a thioester, a monosaccharide, an oligosaccharide, a carbonate or a carbamate, R^2 and R^3 are -H, R^5 is -CH₃, R^7 , R^8 and R^9 are -CH₂-; or
- 5 (000787) (10) R^1 and R^4 independently are -OR^{PR}, -SR^{PR}, -N(R^{PR})₂, an ester, a thioester, a monosaccharide, an oligosaccharide, a carbonate or a carbamate, R^2 is -H, R^3 is -Br, R^5 is -CH₃, R^7 , R^8 and R^9 are -CH₂-; or
- (000788) (11) R^1 and R^4 independently are -OR^{PR}, -SR^{PR}, -N(R^{PR})₂, an ester, a thioester, a monosaccharide, an oligosaccharide, a carbonate or a carbamate, R^2 is
- 10 -H, R^3 is -F, R^5 is -CH₃, R^7 , R^8 and R^9 are -CH₂-; or
- (000789) (12) R^1 and R^4 independently are -OR^{PR}, -SR^{PR}, -N(R^{PR})₂, an ester, a thioester, a monosaccharide, an oligosaccharide, a carbonate or a carbamate, R^2 is -H, R^3 is -OH, R^5 is -CH₃, R^7 , R^8 and R^9 are -CH₂-; or
- (000790) (13) R^1 and R^4 independently are -OR^{PR}, -SR^{PR}, -N(R^{PR})₂, an ester, a
- 15 thioester, a monosaccharide, an oligosaccharide, a carbonate or a carbamate, R^2 and R^3 are -OH, R^5 is -CH₃, R^7 , R^8 and R^9 are -CH₂-; or
- (000791) (14) R^1 and R^4 independently are -OR^{PR}, -SR^{PR}, -N(R^{PR})₂, an ester, a thioester, a monosaccharide, an oligosaccharide, a carbonate or a carbamate, R^2 is -OH, R^3 is -H, -F, -Cl or -Br, R^5 is -CH₃, R^7 , R^8 and R^9 are -CH₂-; or
- 20 (000792) (15) R^1 is -H, R^2 is -OH or =O, R^3 is -OH, -F, -Cl or -Br, R^4 is -OR^{PR}, -SR^{PR}, -N(R^{PR})₂, an ester, a thioester, a monosaccharide, an oligosaccharide, a carbonate or a carbamate, R^5 is -CH₃, R^7 , R^8 and R^9 are -CH₂-; or
- (000793) (16) R^1 and R^2 are -H, R^3 is -OH or =O, -F, -Cl or -Br, R^4 is -OR^{PR}, -SR^{PR}, -N(R^{PR})₂, an ester, a thioester, a monosaccharide, an oligosaccharide, a
- 25 carbonate or a carbamate, R^5 is -CH₃, R^7 , R^8 and R^9 are -CH₂-; or
- (000794) (17) any of (1) through (16) above wherein R^9 is -O- or -NH- instead of -CH₂- or -CH=; or
- (000795) (18) any of (1) through (17) above wherein R^8 is -O- or -NH- instead of -CH₂-; or
- 30 (000796) (19) any of (1) through (18) above wherein R^7 is -O-, -NH- or -CHR¹⁰-CH₂- instead of -CH₂-.

(000797) 22. The method of claim 20 wherein the condition is osteoporosis or a bone fracture and the compound is $3\alpha,17\beta$ -dihydroxy-19-norandrost-4-ene or $3\alpha,17\beta$ -dihydroxy-19-norandrost-5-ene.